Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-4. (canceled)

5. (previously presented) A process for preparing ondansetron hydrochloride monohydrate comprising the steps of:

a) contacting crystals of ondansetron hydrochloride dihydrate with a mixture of from about 4% to about 50% water in ethanol to convert the crystals of ondansetron hydrochloride dihydrate to crystals of ondansetron hydrochloride monohydrate,

b) separating the crystals of ondansetron hydrochloride monohydrate from the ethanol/water mixture, and

c) recovering the crystals of ondansetron hydrochloride monohydrate.

6. (original) The process of claim 5 wherein the contacting occurs at the reflux temperature of the ethanol:water mixture.

7. (original) The process of claim 5 wherein the dihydrate and monohydrate are denominated Form A expressing that their crystal structures are the same.

8. (canceled)

9. (canceled)

10. (currently amended) A process for preparing ondansetron hydrochloride Form A having between about 5% water and about 10% water, comprising the steps of:

a) suspending ondansetron free base in a liquid medium selected from the group consisting of ~~absolute ethanol~~, a mixture of ethanol and isopropanol, ~~and~~ chloroform, and a mixture of chloroform and water,

b) dissolving the free base by adding anhydrous HCl to the suspension,

c) crystallizing ondansetron hydrochloride Form A having between about 5% water and about 10% water from the liquid medium, and

d) separating the crystalline ondansetron hydrochloride Form A having between about 5% water and about 10% water from the liquid medium.

11. (canceled)

12. (original) The process of claim 10 wherein the HCl is added in an amount of 1 ± 0.1 equivalent with respect to the ondansetron free base.

13. (previously presented) The process of claim 10 wherein the anhydrous HCl is a gas.

14. (original) The process of claim 10 wherein the anhydrous HCl is added in solution in an inert organic solvent.

15. (canceled)

16. (currently amended) A process for preparing ondansetron hydrochloride Form A having between about 6 ~~5~~% water and about 9 ~~10~~% water, comprising the steps of:

a) dehydrating crystals of ondansetron hydrochloride dihydrate by contacting the crystals with a liquid medium selected from the group consisting of ethanol, mixtures of ethanol and water, toluene and mixtures of ethanol and toluene,

b) separating the liquid medium from the crystals to obtain ondansetron hydrochloride Form A having between about 6% water and about 9% water, and

c) collecting the crystals of ondansetron hydrochloride Form A having between about 6% water and about 9% water.

17. (original) The process of claim 16 wherein the crystals are mechanically agitated during dehydration.

18. (original) The process of claim 17 wherein the mechanical agitation is sonication.

19. (original) Anhydrous ondansetron hydrochloride.

20. (original) Anhydrous ondansetron hydrochloride Form B.

21. (currently amended) Anhydrous ondansetron hydrochloride ~~polymorphic~~ Form B characterized by powder X-ray diffraction peaks at 10.5, 11.9, 13.0, 13.5, and 15.1 ±0.2 degrees two-theta.

22. (currently amended) The anhydrous ondansetron hydrochloride ~~polymorphic~~ Form B of claim 21, further characterized by powder X-ray diffraction peaks at ~~10.5, 11.9, 13.0, 13.5, 15.1,~~ 20.9, 22.7, 24.0, and 25.7 ±0.2 degrees two-theta.

23. (canceled)

24. (canceled)

25. (currently amended) A process for preparing the anhydrous ondansetron hydrochloride Form B of claim 21 or 22 comprising: ~~by~~

a) treating ondansetron hydrochloride with a dry C_1-C_4 alcohol or ketone [[.]] to form the anhydrous ondansetron hydrochloride Form B of claim 21 or 22; and

b) recovering the anhydrous ondansetron hydrochloride Form B of claim 21 or 22.

26. (original) The process of claim 25 wherein the solvent is absolute ethanol.

27. (currently amended) The process of claim 25 wherein the ondansetron hydrochloride that is treated ~~with dry alcohol~~ is Form A.

28. (original) The process of claim 25 wherein the treatment is carried out at about 20°C.

29. (canceled)

30. (currently amended) The process of claim 25 wherein the alcohol is ethanol, isopropanol, 1-butanol or ~~a~~ mixtures ~~of~~ thereof.

31. (canceled)

32. (currently amended) A process for ~~of~~ preparing the anhydrous ondansetron hydrochloride Form B of claim 21 or 22 comprising: ~~by~~

a) treating ondansetron hydrochloride with a dry organic solvent; and

b) recovering the anhydrous ondansetron hydrochloride Form B of claim 21 or 22.

33. (original) The process of claim 32 wherein the solvent is absolute ethanol.

34. (previously presented) The process of claim 32 wherein the ondansetron hydrochloride that is treated is Form A.

35. (original) The process of claim 32 wherein the solvent is a ketone.

36. (canceled)

37. (original) The process of claim 32 wherein the treatment is carried out at about 20°C.

38. (canceled)

39. (currently amended) The anhydrous ondansetron hydrochloride ~~polymorphic~~ Form B of claim 21 in particle form having 100% of the particles ~~a particle size~~ below about 300 microns in size.

40. (canceled)

41. (currently amended) The anhydrous ondansetron hydrochloride ~~polymorphic~~ Form B of claim 21 in particle form having 100% of the particles ~~a particle size~~ below about 200 microns in size.

42. (canceled)

43. (currently amended) The anhydrous ondansetron hydrochloride ~~polymorphic~~ Form B of claim 21 in particle form having 100% of the particles ~~a particle size~~ below about 40 microns in size.

44. (canceled)

45. (currently amended) The anhydrous ondansetron hydrochloride ~~polymorphic~~ Form B of claim 21 with a water content up to about 2%.

46. (currently amended) A process for ~~preparation of~~ preparing the anhydrous ondansetron hydrochloride ~~polymorphic~~ Form B of claim 21 ~~characterized by powder X-ray diffraction peaks at 10.5, 11.9, 13.0, 13.5, and 15.1 ±0.2 degrees two-theta~~ comprising:

a) reacting HCl gas with a toluene solution of ondansetron base to form the anhydrous ondansetron hydrochloride Form B of claim 21; and

b) recovering the anhydrous ondansetron hydrochloride Form B of claim 21.

47. (previously presented) The process of claim 46 wherein the ondansetron base is dissolved at the reflux temperature of toluene.

48. (previously presented) The process of claim 46 wherein HCl gas is bubbled into the toluene solution of ondansetron base.

49. (currently amended) Ondansetron hydrochloride Form C, characterized by ~~strong~~ powder X-ray diffraction peaks at ~~6.3 and 24.4 ±0.2 degrees two-theta and other peaks at~~ 6.3, 9.2, 10.2, 13.1, ~~and~~ 16.9 and 24.4 ±0.2 degrees two-theta.

50. (currently amended) The ondansetron ~~Ondansetron~~ hydrochloride Form C of claim 49, wherein the ~~characterized by~~ powder X-ray diffraction peaks at 6.3~~, 9.2, 10.2, 13.1, 16.9~~ and 24.4 ±0.2 degrees two-theta are strong peaks.

51. (currently amended) A process for preparing ~~preparation of~~ the ondansetron hydrochloride Form C ~~product~~ of claim 49 or 50 comprising ~~which comprises the steps of~~:

a) dissolving ondansetron base in ethanol,

b) adding an ethanolic solution of ~~hydrochloride~~ hydrogen chloride to form a mixture,

c) filtering the mixture to remove precipitated solids, and

d) evaporating the ethanol ~~mother liquor~~ to recover the ondansetron hydrochloride Form C of claim 49 or 50.

52. (previously presented) Ondansetron hydrochloride Form D, characterized by powder X-ray diffraction peaks at 8.3, 14.0, 14.8 and 25.5 ±0.2 degrees two-theta.

53. (previously presented) A process for preparing the ondansetron hydrochloride Form D of claim 52 comprising the steps of:

a) melting ondansetron hydrochloride in the presence of xylene; and

b) adding the melt to ethanol.

54. (previously presented) The process of claim 53 wherein the ondansetron hydrochloride is ondansetron hydrochloride Form A.

55. (previously presented) The process of claim 53 wherein the ethanol is at a temperature of from about -15°C to about room temperature.

56. (original) The process of claim 55 wherein the ethanol is at a temperature of about -10°C.

57. (currently amended) Ondansetron hydrochloride Form E, characterized by ~~a strong~~ powder X-ray diffraction peaks at ~~7.4 degrees two-theta and peaks at~~ 6.3, 7.4, 10.5, 11.2, 12.3, 13.0, 14.5, 15.9, 17.0, 20.1, 20.8, 24.5, 26.2 and 27.2 ±0.2 degrees two-theta.

58. (currently amended) The ondansetron ~~Ondansetron~~ hydrochloride Form E of claim 57, wherein the ~~characterized by~~ powder X-ray diffraction peaks at ~~6.3,~~

~~7.4, 10.5, 11.2, 12.3, 13.0, 14.5, 15.9, 17.0, 20.1, 20.8, 24.5, 26.2 and 27.2~~ ±0.2 degrees two-theta is a strong peak.

59. (currently amended) A process for preparation of the ondansetron hydrochloride Form E ~~product~~ of claim 57 or 58 comprising: ~~which comprises the step of~~

a) treating ondansetron hydrochloride in isopropanol to form the ondansetron hydrochloride Form E of claim 57 or 58; and

b) recovering the ondansetron hydrochloride Form E of claim 57 or 58.

60. (original) The process of claim 59 wherein the ondansetron hydrochloride is Form A.

61. (original) The process of claim 59 wherein the temperature of the isopropanol is from about room temperature to about reflux temperature.

62. (original) Ondansetron hydrochloride isopropanolate.

63. (original) Ondansetron hydrochloride Form E isopropanolate.

64. (original) Ondansetron hydrochloride Form E mono-isopropanolate.

65. (original) Ondansetron hydrochloride Form E hemi-isopropanolate.

66. (original) Ondansetron hydrochloride Form E having a water content of up to about 10%.

67. (previously presented) Ondansetron hydrochloride Form H, characterized by powder X-ray diffraction peaks at 7.8, 14.0, 14.8 , 24.7 and 25.6 ±0.2 degrees two-theta.

68. (currently amended) A process for preparing the ondansetron hydrochloride Form H of claim 67 comprising ~~which comprises the steps of~~:

a) suspending ~~suspension of~~ ondansetron base in absolute ethanol;

b) adding an ethanol solution of hydrochloric acid to the suspension;

c) precipitating the ondansetron hydrochloride Form H of claim 67 by adding ether to the suspension; and

d) isolating the ondansetron hydrochloride Form H of claim 67.

69. (original) The process of claim 68 wherein the ether is methyl tert-butyl ether or diethyl ether.

70. (original) The process of claim 68 wherein the ether is dry.

71. (canceled)

72. (previously presented) Ondansetron hydrochloride methanolate.

73. (original) Ondansetron hydrochloride methanolate Form I.

74. (currently amended) Ondansetron hydrochloride Form I, characterized by a strong powder X-ray diffraction ~~XRD~~ peak at 25.0 ±0.2 degrees two-theta and other powder X-ray diffraction ~~XRD~~ peaks at 8.2, 9.3, 9.9, 11.1 and 24.9 ±0.2 degrees two-theta.

75. (currently amended) Ondansetron hydrochloride Form I, characterized by a strong powder X-ray diffraction ~~XRD~~ peak at 25.0 ±0.2 degrees two-theta and other powder X-ray diffraction ~~XRD~~ peaks at 8.2, 9.3, 9.9, 11.1, 13.9, 16.0, 17.0, 21.0, 22.6, 25.8, 27.3 and 28.0 ±0.2 degrees two-theta.

76. (currently amended) Ondansetron hydrochloride Form I, characterized by a strong powder X-ray diffraction ~~XRD~~ peak at 25.0 ±0.2 degrees two-theta and other powder X-ray diffraction ~~XRD~~ peaks at 6.9, 8.2, 8.7, 9.1, 9.3, 9.9, 11.1, 11.6, 13.8, 16.1, 16.9, 17.9, 21.1, 22.7, 25.7, 26.6, 27.4 and 27.9 ±0.2 degrees two-theta.

77. (currently amended) A process for preparing ~~crystallizing~~ ondansetron hydrochloride Form I comprising exposing ondansetron hydrochloride to methanol vapor to form ondansetron hydrochloride Form I.

78. (original) The process of claim 77 wherein the exposure is for a period of about three weeks or less.

79. (original) The process of claim 77 wherein the exposure is at room temperature.

80. (original) The process of claim 77 wherein ondansetron hydrochloride Form A is exposed to methanol vapor.

81. (original) The process of claim 77 wherein anhydrous ondansetron hydrochloride Form B is exposed to methanol vapor.

82. (currently amended) A process for preparing anhydrous ondansetron hydrochloride Form B comprising the steps of:

a) dissolving ondansetron base in absolute ethanol;

b) adding to the dissolved ondansetron base an ethanolic solution of hydrogen chloride ~~ethanol/hydrochloric acid solution~~ to obtain anhydrous ondansetron hydrochloride Form B; and

c) collecting by filtration the anhydrous ondansetron hydrochloride Form B.

83. (currently amended) The process of claim 82 wherein the ethanol has no more than 0.5% water ~~is substantially dry~~.

84. (currently amended) The process of claim 82 wherein the ondansetron base and the ethanolic solution of hydrogen chloride ~~ethanol/hydrochloric acid solution~~ are mixed at room temperature.

85. (currently amended) The process of claim 82 wherein the ondansetron base and the ethanolic solution of hydrogen chloride are ~~the mixture of ondansetron base is~~ heated at reflux temperature.

86. (currently amended) The process of claim 82 wherein the ondansetron base and the ethanolic solution of hydrogen chloride ~~ethanol/hydrochloric acid solution~~ are mixed for a period of about 30 to about 70 hours at room temperature.

87. (canceled)

88. (canceled)

89. (currently amended) A pharmaceutical composition comprising the ondansetron hydrochloride of claim 39 ~~in particle form~~ and a pharmaceutically acceptable carrier~~, wherein the ondansetron hydrochloride in particle form has 100% of the particles below about 200 microns in size~~.

90. (currently amended) A pharmaceutical composition comprising the ondansetron hydrochloride of claim 41 ~~in particle form~~ and a pharmaceutically acceptable carrier~~, wherein the ondansetron hydrochloride in particle form has 100% of the particles below about 100 microns in size~~.

91. (currently amended) A pharmaceutical composition comprising the ondansetron hydrochloride of claim 43 ~~in particle form~~ and a pharmaceutically acceptable carrier~~, wherein the ondansetron hydrochloride in particle form has 100% of the particles below about 50 microns in size~~.

92-93. (canceled)